



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Bictegravir (BIC) (Last updated May 22, 2018; last reviewed May 22, 2018)

For additional information see Drugs@FDA: <https://www.accessdata.fda.gov/scripts/cder/daf/>

Formulations

Note: Bictegravir is only available in a fixed-dose combination tablet.

Fixed-Dose Combination Tablet:

- [Biktarvy] Bictegravir 50 mg plus emtricitabine 200 mg plus tenofovir alafenamide (TAF) 25 mg

Dosing Recommendations

[Biktarvy] Bictegravir plus Emtricitabine plus TAF

Pediatric/Adolescent Dose (Aged <18 Years):

- Biktarvy has not been Food and Drug Administration-approved for use in patients aged <18 years.
- *Children Aged <12 Years:* No data on appropriate dose of Biktarvy in children age <12 years.
- *Children and Adolescents (Aged ≥12–18 Years and Weighing ≥35 kg):* 1 tablet once daily. This is an **investigational dose**.

Adult Dose (Aged ≥18 Years):

- 1 tablet once daily in ART-naïve patients. This Biktarvy dose can also be used to replace the current ARV regimen in patients who have been virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable ARV regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy.

Selected Adverse Events

- Diarrhea, nausea, headache

TAF-Associated Adverse Events:

- Increases in low-density lipoprotein cholesterol and total cholesterol levels

Special Instructions

- Administer with or without food.
- Screen patients for hepatitis B virus (HBV) infection before use of emtricitabine or TAF. Severe acute exacerbation of HBV can occur when emtricitabine or TAF is discontinued; therefore, monitor hepatic function for several months after halting therapy with emtricitabine or TAF.
- Biktarvy is not recommended for use with other ARV drugs.
- See the [emtricitabine](#) and [TAF](#) sections of the [Drug Appendix](#) for special instructions and additional information about the individual drug components of Biktarvy.

Metabolism/Elimination

- Bictegravir is metabolized by cytochrome P (CYP) 450 3A and uridine diphosphate glucuronosyltransferase (UGT) 1A1.
- Refer to the [emtricitabine](#) and [TAF](#) sections of the [Drug Appendix](#) for more information on these components of Biktarvy.

Biktarvy Dosing in Patients with Hepatic Impairment:

- Biktarvy **is not recommended** for use in patients with estimated creatinine clearance <30 mL/min.

Biktarvy Dosing in Patients with Renal Impairment:

- Biktarvy **is not recommended** for use in patients with severe hepatic impairment

Drug Interactions (see also the [Adult and Adolescent Guidelines](#) and the [HIV Drug Interaction Checker](#))

- **Metabolism:** Bictegravir is a substrate of cytochrome P 3A and uridine diphosphate glucuronosyltransferase (UGT) 1A1. Tenofovir alafenamide (TAF) is a substrate of P-glycoprotein and UGT1A1. Co-administration of bictegravir/emtricitabine/TAF (a fixed-dose combination [FDC] drug marketed under the brand name Biktarvy) and rifampin is **contraindicated**.^{1,2}
- **Renal effects:** Bictegravir is an inhibitor of OCT2 and MATE1, so it decreases tubular secretion of creatinine. This increases serum creatinine and reduces estimated glomerular filtration rate with no change in glomerular function. Drugs that decrease renal function could reduce clearance of emtricitabine.
- **Absorption:** Administering bictegravir concurrently with antacids lowers the plasma concentrations of bictegravir. This is due to formation of complexes in the gastrointestinal tract, and not because of changes in gastric pH. It is best to administer Biktarvy, which contains bictegravir, at least 2 hours, but preferably 4 hours, before administering antacids. Chelation by high concentrations of divalent cations, such as iron, decreases absorption of integrase strand transfer inhibitors (INSTIs), including elvitegravir and bictegravir. For this reason, Biktarvy should be administered at least 4 hours before or after iron supplements or multivitamins containing iron. Biktarvy **is not recommended** for use with other antiretroviral (ARV) drugs.

Major Toxicities

- **More common:** Diarrhea, nausea, headache. In two clinical trials, total bilirubin increased by up to 2.5 times the upper limit of normal in 12% of patients who received Biktarvy. In general, however, bilirubin increases were quite mild and did not lead to drug discontinuations in these trials.² Creatine kinase elevations can occur.
- **Less common (more severe):** Severe immune reconstitution inflammatory syndrome may be more common with INSTIs than with other ARV agents.

Resistance

The International Antiviral Society-USA (IAS-USA) maintains a [list of updated resistance mutations](#) and the [Stanford University HIV Drug Resistance Database](#) offers a discussion of each mutation. Bictegravir, dolutegravir, and cabotegravir, the “second-generation” INSTIs, have higher barriers to resistance than the first-generation INSTIs raltegravir and elvitegravir^{3,4} and may have more activity against non-B subtypes of HIV-1.⁵

Pediatric Use

Approval

Bictegravir is not approved for use in children or adolescents. Bictegravir was Food and Drug Administration-approved in 2018 for use in adults who have no ARV treatment history. It is also approved to replace the current ARV regimen in patients who have been virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable ARV regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of the FDC product Biktarvy, which contains 50 mg of bictegravir, 200 mg of emtricitabine, and 25 mg of TAF.²

Efficacy in Clinical Trials

In a short-term Phase 1 study, bictegravir monotherapy at doses of 50 mg or 100 mg was well tolerated and led to HIV-1 RNA <50 copies/mL within 11 days in three out of eight participants in both of these dosing groups.⁶ Two Phase 3 randomized trials in ARV treatment-naïve adults showed that Biktarvy had similar efficacy (viral load suppression [VLS] to HIV-1 RNA <50 copies/mL) and safety (incidence of study drug discontinuation [SDD] or death) to comparator regimens. VLS occurred in 89% of participants who received coformulated bictegravir 50 mg, emtricitabine 200 mg, and TAF 25 mg (BIC/FTC/TAF; N = 320) and in 93% of participants who received a regimen of dolutegravir/emtricitabine 50 mg/200 mg and TAF 25 mg (N = 325). SDD occurred in 1% of participants in both groups. In a separate trial, VLS occurred in 92% of participants who received BIC/FTC/TAF (N = 314) and in 93% of participants who received coformulated abacavir/dolutegravir/lamivudine (ABC/DTG/3TC) 600 mg/50 mg/300 mg (N = 315). SDD was not reported for any of the participants receiving

BIC/FTC/TAF, though SDD did occur in 1% of participants receiving ABC/DTG/3TC.^{2,8} Studies that randomized virologically suppressed patients on stable ARV regimens to either continue their current regimens or switch to coformulated BIC/FTC/TAF have shown that BIC/FTC/TAF has similar safety and efficacy to existing regimens. VLS occurred in 94% of participants who were randomized to switch to BIC/FTC/TAF (N = 282) and in 95% of participants who continued taking ABC/DTG/3TC (N = 281). SDD was reported in 2% of participants and 1% of participants, respectively. Ninety-two percent of participants who were randomized to switch to BIC/FTC/TAF (N = 290) achieved VLS, while 89% of participants who continued receiving atazanavir- or darunavir-based combination ARV regimens (N = 287) achieved VLS. SDD occurred in 1% of participants in both of these groups.²

Formulations

Bictegravir is only available in the coformulated tablet Biktarvy, which contains bictegravir, emtricitabine, and TAF.

Use of Biktarvy in Adolescents Aged 12 Years to 18 Years

The adult dosage formulation of Biktarvy (BIC/FTC/TAF 50 mg/200 mg/25 mg) was administered to adolescents aged 12 to <18 years and weighing ≥ 35 kg who had had viral loads <50 copies/mL for ≥ 6 months. The drug was well tolerated, and all of the 24 participants in the study had viral loads <50 copies/mL at Week 24.⁹

Use of Biktarvy in Children Aged 6 Years to <12 Years

Studies of the adult dosage formulation of Biktarvy are underway in this age group.

References

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